Listing of Claims

1. (Currently amended) A method of analyzing a biological specimen, comprising:

placing the biological specimen on a substrate with one or more different capture regions, wherein the one or more different capture regions of the substrate contain different identification molecules that interact with different biological molecules from the biological specimen; and

transferring components of the biological specimen through the one or more different capture regions under conditions that allow the components to interact with the different identification molecules in the different capture regions of the substrate to produce a pattern that is informative about ~~the identification of~~ the biological molecule,

thereby analyzing the biological specimen.

2. (Original) The method of claim 1, wherein the different capture regions of the substrate are layers.

3. (Original) The method of claim 1, wherein the biological specimen is a cellular specimen.

4. (Original) The method of claim 1, wherein the different capture regions of the substrate are layers, and the biological specimen is a cellular specimen.

5. (Original) The method of claim 4, wherein the layers are contiguous, and components of the cellular specimen are transferred through the different layers of the substrate by capillary action of the substrate.

6. (Original) The method of claim 4, wherein the layered substrate comprises contiguous porous layers that exert capillary pressure on the cellular specimen.

7. (Original) The method of claim 4, wherein the components of the cellular specimen are transferred through the different layers of the substrate by electrophoresis.

8. (Original) The method of claim 4, wherein the components maintain a cellular architecture of the specimen as the components are transferred through the layers of the substrate.

9. (Original) The method of claim 8, further comprising correlating interaction between different identification molecules and the components of the cellular specimens, with a cellular architecture of the specimen.

10. (Original) The method of claim 4, further comprising placing multiple different discrete cellular specimens on a surface of the substrate, wherein a correspondence is maintained between the multiple discrete cellular specimens and particular transferred components.

11. (Original) The method of claim 10 wherein at least 20 different cellular specimens are placed on the surface of the substrate.

12. (Original) The method of claim 4, wherein the cellular specimen is a section of a tissue specimen.

13. (Original) The method of claim 12, wherein the cellular specimen is a section of a tumor.

14. (Original) The method of claim 4, further comprising correlating a pattern of interactions of different identification molecules in the different layers of the substrate with a component having a known identity.

15. (Original) The method of claim 4, wherein there are at least 10 layers of the substrate.

16. (Original) The method of claim 15, wherein there are at least 100 layers of the substrate.

17. (Original) The method of claim 4, wherein the layers of the substrate have a thickness of at least about 25 μm.

18. (Original) The method of claim 4, wherein the identification molecules are antibodies that interact with the components of the cellular specimen.

19. (Original) The method of claim 4, wherein the identification molecules interact with different cellular regions of the cellular specimen, and interaction of the identification molecules is correlated with a region of the cellular specimen.

20. (Original) The method of claim 4, wherein the cellular specimen is placed on a surface of the layered substrate prior to transferring components of the cellular specimen through the substrate.

21. (Original) The method of claim 4, wherein the specimen is treated, prior to transferring components of the cellular specimen through the layers, to selectively transfer components through the layers.

22. (Original) The method of claim 21, wherein the specimen is placed on a surface of the layered substrate in a gel, and a concentration of the gel is varied to selectively transfer components of different molecular size.

23. (Original) The method of claim 22, wherein a high concentration gel is used to selectively transfer proteins of a relatively smaller molecular size.

24. (Currently amended) The method of claim 4, comprising identifying the ~~component~~ components of the specimen by determining which identification ~~molecule~~ molecules the ~~component interacts~~components interact with.

25. (Original) The method of claim 24, further comprising reacting an identified component with a second identification molecule, to determine whether the identified component is associated with an other component.

26. (Original) The method of claim 25, wherein the cellular specimen is a tumor specimen, and the identified component is an intact protein, and identification of the other component is used to determine whether a second protein is associated with the protein in the tumor.

27. (Original) The method of claim 26, wherein multiple tumor specimens are placed on the substrate, and components of the multiple tumor specimens are simultaneously separately transferred through the substrate.

28. (Original) The method of claim 27, wherein the multiple tumor specimens are specimens of a particular type of tumor at different stages of tumor progression.

29. (Original) The method of claim 28, wherein the multiple tumor specimens are specimens of a tumor from a particular subject at different stages of tumor progression in that subject.

30. (Original) The method of claim 4, wherein the cellular specimen is obtained by dissecting a cell population of interest from a larger cell population.

31. (Original) The method of claim 30, wherein dissecting a cell population of interest comprises laser capture microdissection of the cell population.

32. (Original) The method of claim 4, wherein the cellular specimen comprises a cell lysate from a cell population of interest.

33. (Original) The method of claim 4, wherein one or more of the layers is an electrically conductive layer.

34. (Original) The method of claim 33, wherein the layers are separable, and are separated after transferring the components of the cellular specimen, for individualized identification of the components of the cellular specimen retained in each separated layer.

35. (Original) The method of claim 33 wherein the each layer is selected from the group consisting of a high concentration agarose gel, a low concentration agarose gel, a high concentration polyacrylamide gel, a low concentration polyacrylamide gel, and a membrane.

36. (Original) The method of claim 4 wherein the identification molecules are molecules selected from the group consisting of antibodies, nucleic acids, peptides, receptors, and ligands.

37. (Original) The method of claim 4 wherein the identification molecule comprises a capture molecule which retains a component of the cellular specimen in the layer, the method further comprising exposing the identification molecule to a detection molecule that associates with a combination of the capture molecule and the component of the sample, or associates with a region of the component different than a region that is recognized by the identification molecule.

38. (Original) The method of claim 37, wherein the component is a protein, the identification molecule recognizes a first domain of the protein, and the detection molecule recognizes the different region of the protein.

39. (Original) The method of claim 38, wherein the detection molecule is selected from the group consisting of antibodies, nucleic acids, peptides, receptors, ligands and stains.

40. (Original) The method of claim 4, wherein the identification molecules capture components of the transferred components in relative abundance to a quantity of the components in the cellular specimen, and provide a quantitative indication of the relative abundance of the components in the cellular specimen.

41. (Original) The method of claim 4, wherein the cellular specimen is selected from the group consisting of a tissue section, cultured cells, and a cytology sample.

42. (Previously presented) The method of claim 1, wherein the transferred components that interact with the different identification molecules comprise intact proteins or intact nucleic acid molecules that have not been subjected to proteolytic or nucleolytic reactions prior to transfer through the different layers of the substrate.

43. (Previously presented) The method of claim 1, further comprising capturing a component of the components of the cellular specimens, and performing mass spectroscopy sequencing to identify the captured component.

44. (Currently amended) The method of claim 1, wherein transferring components of the ~~cellular~~ biological specimen through the layered substrate produces a three dimensional matrix, wherein a surface of the substrate on which the ~~cellular~~ biological specimen is placed provides a two dimensional cytocoherent matrix, and a third dimension is provided by transfer of components of the ~~cellular~~ biological specimens through the different layers, wherein there is an identifiable correspondence between a position of the component of the ~~cellular~~ biological specimen in the two dimensional cytocoherent matrix and a position of the transferred components in the three dimensional matrix.

45. (Canceled)

46. (Original) A method of analyzing a cellular specimen, comprising:

providing a substrate comprising a plurality of different layers having contiguous faces, each layer including a corresponding capture molecule capable of interacting with and capturing a component of the cellular specimen;

applying the cellular specimen to a face of the substrate, and transferring intact components of the specimen through the contiguous faces of the different layers of the matrix;

reacting the intact components of the specimen with the capture molecule; and

correlating a pattern of capture in the different layers with information about the cellular specimen.

47. (Original) The method of claim 46, wherein the capture molecule captures the component in an amount that corresponds to a quantity of the component in the cellular specimen.

48. (Original) The method of claim 46, wherein the intact components comprise one or more of proteins or nucleic acids that have not been subjected to a proteolytic or nucleolytic processing step.

49. (Currently amended) The method of claim 46, wherein applying the cellular ~~substrate~~ specimen to a face of the substrate comprises applying multiple different cellular specimens to the face of the substrate.

50. (Original) The method of claim 46, wherein the pattern of capture comprises a three dimensional matrix, in which a pattern of the cellular specimen applied to the face of the substrate forms a cytocoherent two dimensional matrix, and a pattern of capture in the different layers forms a third dimension, wherein there is a correspondence between the cytocoherent two dimensional matrix and the third dimension, such that the pattern of capture can be correlated to specific cellular architecture in the cellular specimen.

51. (Original) The method of claim 46, wherein transferring intact components of the specimen comprises introducing an electrical current through the contiguous faces of the substrate, so that the current flows transverse to the plurality of different layers.

52. (Original) The method of claim 51, wherein the plurality of different layers comprises a plurality of contiguous electrically conductive gels through which the electrical current is conducted.

53. (Original) The method of claim 46, wherein transferring intact components of the specimen comprises transferring by capillary action.

54. (Original) The method of claim 53, wherein the plurality of different layers comprise contiguous nitrocellulose layers that exert capillary pressure on the cellular specimen.

55-66. (Canceled)

67. (Previously presented) The method of claim 2, wherein the transferred components that interact with the different identification molecules comprise intact proteins or intact nucleic acid molecules that have not been subjected to proteolytic or nucleolytic reactions prior to transfer through the different layers of the substrate.

68. (Previously presented) The method of claim 2, further comprising capturing a component of the components of the cellular specimens, and performing mass spectroscopy sequencing to identify the captured component.

69. (Currently amended) The method of claim 2, wherein transferring components of the ~~cellular~~ biological specimen through the layered substrate produces a three dimensional matrix, wherein a surface of the substrate on which the cellular specimen is placed provides a two dimensional cytocoherent matrix, and a third dimension is provided by transfer of components of the ~~cellular~~ biological specimens through the different layers, wherein there is an identifiable correspondence between a position of the component of the ~~cellular~~ biological specimen in the two dimensional cytocoherent matrix and a position of the transferred components in the three dimensional matrix.